10/002,292

SGM 6938.1
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent of: Ward et al.
Patent No.: 6,902,914 B2
Issued: June 7, 2005
Confirmation No.: 2146
For: RECOMBINANT DNA PROCESSES USING A DNTP MIXTURE CONTAINING MODIFIED NUCLEOTIDES

November 30, 2005

REQUEST FOR EXPEDITED ISSUANCE OF CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322

TO THE COMMISSIONER FOR PATENTS,

SIR:

On studying the above-identified patent, the following errors were found (these errors are also noted on the attached form PTO-1050):

Column 2, line 2: "5" should read - - - 5' - - -.

Column 3, line 56: "using the an" should read - - - using an - - -.

Column 6, line 55: "5" should read - - - 5' - - -.

Column 11, line 64: "th" should read - - - the - - -.

Column 19, line 29: "100,000" should read - - - 100,000 times - - -.

Column 22, line 7: "MS" should read - - - M5 - - -.

Column 23, line 29: "furthers contain" should read - - - further contains - - -.

Column 25, line 56: "restrioction" should read - - - restriction - - -.

Column 27, line 16: "DAMP" should read - - - dAMP - - -.

Column 32, line 31: "genes" should read - - - gene's - - -.

Column 35, Seq. No. 10 <223>: "RECOMBINANY" should read - - - RECOMBINANT - - -.

12/05/2005 LWONDIM2 00000029 6902914
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Column 37, Seq. No. 11 <223>: "promotoer" should read - - - promoter - - -.

Column 37, Seq. No. 11 <223>: "promotoer" should read - - - promoter - - -.

Column 39, claim 1, line 12: "UTP" should read - - - dUTP - - -.

Column 39, claim 1, line 17: "the" should read - - - a - - -.

Column 39, claim 1, line 21: "UTP" should read - - - dUTP - - -.

Column 42, claim 36, line 53: "thereof" should read - - - thereof; - - -.

Column 43, claim 37, line 11: "UTP" should read - - - dUTP - - -.

Column 43, claim 37, line 19: "UTP" should read - - - dUTP - - -.

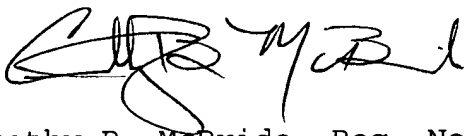
REMARKS

In accordance with 37 CFR 1.322, a copy of Amendment B, dated January 20, 2005, and a copy of the Notice of Allowance dated February 2, 2005, are attached.

Since one or more of the errors shown above were made by Applicants, the $100.00 fee required under Rule 1.323 is enclosed.

We respectfully request that a certificate of correction be issued.

Respectfully submitted,



Timothy B. McBride, Reg. No. 47,781
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One Metropolitan Square, 16th Floor
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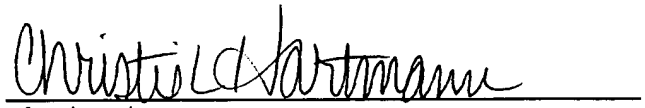
CERTIFICATE OF MAILING

I hereby certify that the foregoing Letter to the Patent and Trademark Office in the patent of Ward et al., Patent No. 6,902,914 B2, issued June 7, 2005 is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Post Issue, Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on this 30th day of November, 2005.



Christie L. Hartmann

TBM/clh
*Enclosure

PTO/SB/44 (04-05)
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SGM 6938.1
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Brian Ward et al.
Serial No. : 10/002,292
Filed : November 15, 2001
Confirmation No. 2146
For RECOMBINANT DNA PROCESSES USING A dNTP MIXTURE CONTAINING MODIFIED NUCLEOTIDES
Examiner : Horlick, Kenneth R.

Art Unit 1637

EV453249674US

Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

January 20, 2005

AMENDMENT B

Sir:

In response to the Final Office Action mailed October 20, 2004, please enter the following amendments and consider the following remarks.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 17 of this paper.

Conclusion begins on page 18 of this paper.

LISTING OF CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-185 (cancelled)

186. (currently amended) ~~The kit of claim 159 wherein the mixture comprises~~ **A kit for directionally ligating a double-stranded nucleic acid to a first adaptor sequence, the kit comprising**:

(A) a first unmodified deoxynucleotidetriphosphate and modified deoxynucleotidetriphosphate pair, unmodified $dNTP_1$ and modified $dNTP_1$, respectively, selected from the group consisting of (1) ~~the~~ **an** unmodified dATP and ~~the~~ **a** modified dATP, (2) ~~the~~ **an** unmodified dGTP and ~~the~~ **a** modified dGTP, (3) ~~the~~ **an** unmodified dCTP and **a** modified dCTP, (4) **an** unmodified dTTP and **a** modified dTTP, and (5) **an** unmodified dUTP and ~~the~~ **a** modified UTP;

(B) a second unmodified deoxynucleotidetriphosphate and modified deoxynucleotidetriphosphate pair, unmodified $dNTP_2$ and modified $dNTP_2$, respectively, selected from the group consisting of (1) ~~the~~ **an** unmodified dATP and the modified dATP, (2) ~~the~~ **an** unmodified dGTP and ~~the~~ **a** modified dGTP, (3) ~~the~~ **an** unmodified dCTP and ~~the~~ **a** modified dCTP, (4) ~~the~~ **an** unmodified dTTP and ~~the~~ **a** modified dTTP, and (5) ~~the~~ **an** unmodified dUTP and ~~the~~ **a** modified UTP, wherein said first and second pairs are different; and

(C) **instructions for using the deoxynucleotidetriphosphate mixture in a procedure for directionally ligating a nucleic acid into a first adaptor sequence, wherein the adaptor sequence is a duplex nucleotide sequence for cohesive ligation to an end of an exonuclease digested amplification product;**

wherein (1) said first and second pairs are different, (2) the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is less than 51**; (3) the unmodified dATP is selected from the group consisting of dATP and analogs thereof, the unmodified dGTP is selected from the group consisting of dGTP and analogs thereof, the unmodified dCTP is selected from the group consisting of dCTP and analogs thereof, the unmodified dTTP is selected from the group consisting of dTTP and analogs thereof, and the unmodified dUTP is selected from the group consisting of dUTP and analogs thereof, (4) the analogs of dATP, dGTP, dCTP, dTTP, and dUTP do not impart resistance against enzymatic degradation by an exonuclease relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, when incorporated into a polynucleotide, and (5) the modified dATP, modified dGTP, modified dCTP, modified dTTP, or modified dUTP when incorporated into a polynucleotide imparts resistance, relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, against enzymatic degradation by an exonuclease at the site of incorporation**.

187. (previously presented) The kit of claim 186 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is less than 27.

188. (previously presented) The kit of claim 187 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is less than 13.

189. (previously presented) The kit of claim 186 wherein the modified $dNTP_1$ and the modified $dNTP_2$ are alpha phosphate substituted deoxynucleotidetriphosphates.

190. (previously presented) The kit of claim 189 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is between about 0.05 and 6.4.

191. (previously presented) The kit of claim 190 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is between about 0.1 and 3.2.

192. (previously presented) The kit of claim 191 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is between about 0.2 and 1.6.

193. (previously presented) The kit of claim 190 wherein the unmodified $dNTP_1$ is the unmodified dGTP, the unmodified $dNTP_2$ is the unmodified dATP, the modified $dNTP_1$ is an alpha thiophosphorano dGTP, and the modified $dNTP_2$ is an alpha thiophosphorano dATP.

194. (previously presented) The kit of claim 186 wherein the modified $dNTP_1$ and the modified $dNTP_2$ are alpha thiophosphorano deoxynucleotidetriphosphates.

195. (previously presented) The kit of claim 194 wherein the unmodified $dNTP_1$ is the unmodified dGTP, the unmodified $dNTP_2$ is the unmodified dATP, the modified $dNTP_1$ is an alpha thiophosphorano dGTP, and the modified $dNTP_2$ is an alpha thiophosphorano dATP.

196. (previously presented) The kit of claim 195 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.8 and 5.3.

197. (previously presented) The kit of claim 195 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.17 and 2.7.

198. (previously presented) The kit of claim 197 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.33 and 1.33.

199. (previously presented) The kit of claim 198 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is about 0.66.

200. (previously presented) The kit of claim 186 wherein the modified $dNTP_1$ and the modified $dNTP_2$ are alpha boranophosphorano deoxynucleotidetriphosphates.

201. (previously presented) The kit of claim 200 wherein the unmodified $dNTP_1$ is the unmodified dGTP, the unmodified $dNTP_2$ is the unmodified dATP, the modified $dNTP_1$ is an alpha boranophosphorano dGTP, and the modified $dNTP_2$ is an alpha boranophosphorano dATP.

202. (previously presented) The kit of claim 201 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.05 and 6.4.

203. (previously presented) The kit of claim 202 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.1 and 3.2.

204. (previously presented) The kit of claim 203 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.2 and 1.6.

205. (previously presented) The kit of claim 204 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is about 0.4.

206. (currently amended) **A kit for directionally ligating a double-stranded nucleic acid to a first adaptor sequence, the kit comprising:** ~~The kit of claim 159 further comprising~~

(A) a deoxynucleotidetriphosphate mixture comprising:

(1) (a) an unmodified dATP selected from the group consisting of dATP and analogs thereof, (b) an unmodified dGTP selected from the group consisting of dGTP and analogs thereof, (c) an unmodified dCTP selected from the group consisting of dCTP and analogs thereof, and (d) (i) an unmodified dTTP selected from the group consisting of dTTP and analogs thereof, or (ii) an unmodified dUTP selected from the group consisting of dUTP and analogs thereof; and

(2) at least one modified deoxynucleotidetriphosphate selected from the group consisting of a modified dATP, a modified dGTP, a modified dCTP, a modified dTTP, and a modified dUTP;

(B) a first adaptor sequence, wherein the first adaptor sequence comprises a nucleotide sequence encoding at least one epitope tag~~.~~**; and**

(C) instructions for using the deoxynucleotidetriphosphate mixture in a procedure for directionally ligating a nucleic acid into the first adaptor sequence;

wherein (1) the analogs of dATP, dGTP, dCTP, dTTP, and dUTP do not impart resistance against enzymatic degradation by an exonuclease relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, when incorporated into a polynucleotide; (2) the modified dATP, modified dGTP, modified dCTP, modified dTTP, or modified dUTP when incorporated into a polynucleotide imparts resistance, relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, against enzymatic degradation by an exonuclease at the site

of incorporation; and (3) the adaptor sequence is a duplex nucleotide sequence for cohesive ligation to an end of an exonuclease digested amplification product.

207. (previously presented) The kit of claim 206 wherein the first adaptor sequence comprises an epitope tag selected from the group consisting of c-myc, polyhistidine, polyarginine, glutathione-S-transferase (GST) tag, HA epitope, V5, and DYKDDDDK.

208. (previously presented) The kit of claim 207 wherein the first adaptor sequence comprises a DYKDDDDK epitope tag.

209. (previously presented) The kit of claim 206 further comprising a second adaptor sequence.

210. (previously presented) The kit of claim 209 wherein the second adaptor sequence comprises a nucleotide sequence encoding at least one epitope tag and the epitope tag comprises c-myc, polyhistidine, polyarginine, glutathione-S-transferase (GST) tag, HA epitope, V5, or sequence DYKDDDDK.

211. (previously presented) The kit of claim 210 wherein at least one epitope tag of the second adaptor sequence comprises the sequence DYKDDDDK.

212-214. (cancelled)

215. (currently amended) **A kit for directionally ligating a double-stranded nucleic acid to a first adaptor sequence, the kit comprising:** ~~**The kit of claim 159 further comprising**~~

(A) a deoxynucleotidetriphosphate mixture comprising:

(1) (a) an unmodified dATP selected from the group consisting of dATP and analogs thereof, (b) an unmodified dGTP selected from the group

consisting of dGTP and analogs thereof, (c) an unmodified dCTP selected from the group consisting of dCTP and analogs thereof, and (d) (i) an unmodified dTTP selected from the group consisting of dTTP and analogs thereof, or (ii) an unmodified dUTP selected from the group consisting of dUTP and analogs thereof; and

(2) at least one modified deoxynucleotidetriphosphate selected from the group consisting of a modified dATP, a modified dGTP, a modified dCTP, a modified dTTP, and a modified dUTP;

(B) a first primer and a second primer; and

(C) instructions for using the deoxynucleotidetriphosphate mixture in a procedure for directionally ligating a nucleic acid into a first adaptor sequence;

wherein (1) the analogs of dATP, dGTP, dCTP, dTTP, and dUTP do not impart resistance against enzymatic degradation by an exonuclease relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, when incorporated into a polynucleotide; (2) the modified dATP, modified dGTP, modified dCTP, modified dTTP, or modified dUTP when incorporated into a polynucleotide imparts resistance, relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, against enzymatic degradation by an exonuclease at the site of incorporation; (3) a the first primer is complimentary to a first strand of the double-stranded nucleic acid~~, the first primer having~~ and has a first terminus complimentary to a first ligation site sequence of the first adaptor sequence~~,~~ ~~and~~; (4) a the second primer is complimentary to a second strand of the double-stranded nucleic acid~~, the second primer having~~ and has a second terminus complimentary to a second ligation site sequence of a second adaptor sequence; (5) ~~wherein~~ the first terminus of the first primer and the second terminus of the second primer are not identical; and (6) each adaptor sequence is a duplex nucleotide sequence for cohesive ligation to an end of an exonuclease digested amplification product.

216. (previously presented) The kit of claim 215 wherein the first terminus or the second terminus is about one to about ten nucleotides in length.

217. (previously presented) The kit of claim 216 wherein the first terminus or the second terminus is two to seven nucleotides in length.

218. (previously presented) The kit of claim 217 wherein the first terminus or the second terminus is two to five nucleotides in length.

219. (previously presented) The kit of claim 218 wherein the first terminus or the second terminus is four nucleotides in length.

220. (previously presented) The kit of claim 215 wherein the first terminus is a 3' terminus and the second terminus is a 3' terminus.

221. (previously presented) The kit of claim 215 wherein the first terminus is a 5' terminus and the second terminus is a 5' terminus.

222. (previously presented) The kit of claim 221 wherein the first terminus is four nucleotides in length, the second terminus is four nucleotides in length, and the first terminus and the second terminus are not identical.

223-227. (cancelled)

228. (previously presented) The kit of claim 215 further comprising instructions for using the deoxynucleotidetriphosphate mixture in a procedure for directionally ligating the nucleic acid into a second adaptor sequence.

229. (**currently amended**) A deoxynucleotidetriphosphate mixture comprising:
(A) (1) an unmodified dATP selected from the group consisting of dATP and analogs thereof, (2) an unmodified dGTP selected from the group consisting of

dGTP and analogs thereof, (3) an unmodified dCTP selected from the group consisting of dCTP and analogs thereof, and (4) (a) an unmodified dTTP selected from the group consisting of dTTP and analogs thereof, or (b) an unmodified dUTP selected from the group consisting of dUTP and analogs thereof~~, wherein the analogs of dATP, dGTP, dCTP, dTTP, and dUTP do not impart resistance against enzymatic degradation by an exonuclease relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, when incorporated into a polynucleotide;~~ and

(B) at least two modified deoxynucleotidetriphosphates selected from the group consisting of a modified dATP, a modified dGTP, a modified dCTP, a modified dTTP, and a modified dUTP~~; wherein the modified dATP, modified dGTP, modified dCTP, modified dTTP, or modified dUTP when incorporated into a polynucleotide imparts resistance, relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, against enzymatic degradation by an exonuclease at the site of incorporation.~~

wherein (1) the analogs of dATP, dGTP, dCTP, dTTP, and dUTP do not impart resistance against enzymatic degradation by an exonuclease relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, when incorporated into a polynucleotide; and (2) the modified dATP, modified dGTP, modified dCTP, modified dTTP, or modified dUTP when incorporated into a polynucleotide imparts resistance, relative to dATP, dGTP, dCTP, dTTP, and dUTP, respectively, against enzymatic degradation by an exonuclease at the site of incorporation.

230. (**currently amended**) The dNTP mixture of claim 229 wherein the mixture comprises:

(A) a first unmodified deoxynucleotidetriphosphate and modified deoxynucleotidetriphosphate pair, unmodified $dNTP_1$ and modified $dNTP_1$, respectively, selected from the group consisting of (1) the unmodified dATP and the modified dATP, (2) the unmodified dGTP and the modified dGTP, (3) the

unmodified dCTP and the modified dCTP, (4) the unmodified dTTP and the modified dTTP, and (5) the unmodified dUTP and the modified UTP; and

(B) a second unmodified deoxynucleotidetriphosphate and modified deoxynucleotidetriphosphate pair, unmodified $dNTP_2$ and modified $dNTP_2$, respectively, selected from the group consisting of (1) the unmodified dATP and the modified dATP, (2) the unmodified dGTP and the modified dGTP, (3) the unmodified dCTP and the modified dCTP, (4) the unmodified dTTP and the modified dTTP, and (5) the unmodified dUTP and the modified UTP_2;

wherein said first and second pairs are different; **and** ~~**wherein**~~ the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is less than 51.

231. (previously presented) The mixture of claim of 230 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is less than 27.

232. (previously presented) The mixture of claim 231 wherein the ratio of the modified $dNTP_1$ to the modified $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is less than 13.

233. (previously presented) The mixture of claim 230 wherein the modified $dNTP_1$ and the modified $dNTP_2$ are alpha phosphate substituted deoxynucleotidetriphosphates.

234. (previously presented) The mixture of claim 233 wherein the ratio of the alpha phosphate substituted $dNTP_1$ to the alpha phosphate substituted $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is between 0.05 and 6.4.

235. (previously presented) The mixture of claim 234 wherein the ratio of the alpha phosphate substituted $dNTP_1$ to the alpha phosphate substituted $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is between 0.1 and 3.2.

236. (previously presented) The mixture of claim 235 wherein the ratio of the alpha phosphate substituted $dNTP_1$ to the alpha phosphate substituted $dNTP_2$ relative to the unmodified $dNTP_1$ to the unmodified $dNTP_2$ is between 0.2 and 1.6.

237. (previously presented) The mixture of claim 234 wherein the unmodified $dNTP_1$ is the unmodified dGTP, the unmodified $dNTP_2$ is the unmodified dATP, the modified $dNTP_1$ is an alpha thiophosphorano dGTP, and the modified $dNTP_2$ is an alpha thiophosphorano dATP.

238. (previously presented) The mixture of claim 233 wherein the modified $dNTP_1$ and the modified $dNTP_2$ are alpha thiophosphorano deoxynucleotidetriphosphates.

239. (previously presented) The mixture of claim 238 wherein the unmodified $dNTP_1$ is the unmodified dGTP, the unmodified $dNTP_2$ is the unmodified dATP, the modified $dNTP_1$ is an alpha thiophosphorano dGTP, and the modified $dNTP_2$ is an alpha thiophosphorano dATP.

240. (previously presented) The mixture of claim 239 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.8 and 5.3.

241. (previously presented) The mixture of claim 239 wherein the ratio of alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.17 and 2.7.

242. (previously presented) The mixture of claim 241 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.33 and 1.33.

243. (previously presented) The mixture of claim 242 wherein the ratio of the alpha thiophosphorano dGTP to the alpha thiophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is about 0.66.

244. (previously presented) The mixture of claim 233 wherein the modified $dNTP_1$ and the modified $dNTP_2$ are alpha boranophosphorano deoxynucleotidetriphosphates.

245. (previously presented) The mixture of claim 244 wherein the unmodified $dNTP_1$ is the unmodified dGTP, the unmodified $dNTP_2$ is the unmodified dATP, the modified $dNTP_1$ is an alpha boranophosphorano dGTP, and the modified $dNTP_2$ is an alpha boranophosphorano dATP.

246. (previously presented) The mixture of claim 245 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.05 and 6.4.

247. (previously presented) The mixture of claim 246 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.1 and 3.2.

248. (previously presented) The mixture of claim 247 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is between 0.2 to 1.6.

249. (previously presented) The mixture of claim 248 wherein the ratio of the alpha boranophosphorano dGTP to the alpha boranophosphorano dATP relative to the unmodified dGTP to the unmodified dATP is about 0.4.

250. (**currently amended**) A kit for directionally ligating a double-stranded nucleic acid to a first adaptor sequence, the kit comprising:

(A) a deoxynucleotidetriphosphate (dNTP) mixture, the dNTP mixture comprising modified dNTPs for at least one of the four nucleotide triphosphates comprising dATP, dGTP, dCTP, dTTP and analogs thereof, which, when incorporated into a polynucleotide, impart resistance against enzymatic degradation by an exonuclease at the site of incorporation of the modified dNTPs; and

(B) a first adaptor sequence~~, wherein the first adaptor sequence comprises~~ **comprising** a nucleotide sequence encoding at least one epitope tag; and

(C) instructions for using the deoxynucleotidetriphosphate mixture in a procedure for directionally ligating a nucleic acid into a first adaptor sequence.

251. (previously presented) The kit of claim 250 wherein the first adaptor sequence comprises an epitope tag selected from the group consisting of c-myc, polyhistidine, polyarginine, glutathione-S-transferase (GST) tag, HA epitope, V5, and DYKDDDDK.

252. (previously presented) The kit of claim 251 wherein the first adaptor sequence comprises a DYKDDDDK epitope tag.

253. (previously presented) A kit for directionally ligating a double-stranded nucleic acid to a first adaptor sequence, the kit comprising:

(A) a deoxynucleotidetriphosphate mixture comprising:

(1) (a) dATP, (b) dGTP, (c) dCTP, and (d) dTTP; and

(2) at least one modified deoxynucleotidetriphosphate selected from the group consisting of a modified dATP, a modified dGTP, a modified dCTP, a modified dTTP, and a modified dUTP wherein the modified dATP, modified dGTP, modified dCTP, or modified dTTP when incorporated into a polynucleotide imparts resistance, relative to dATP, dGTP, dCTP, and dTTP, respectively, against enzymatic degradation by an exonuclease at the site of incorporation;

(B) a first primer complimentary to a first strand of the double-stranded nucleic acid, the first primer having a first terminus complimentary to a first ligation site sequence of the first adaptor sequence;

(C) a second primer complimentary to a second strand of the double-stranded nucleic acid, the second primer having a second terminus complimentary to a second ligation site sequence of a second adaptor sequence, wherein the first terminus of the first primer and the second terminus of the second primer are not identical;

(D) an exonuclease;

(E) at least one polymerase; and

(F) instructions for using the deoxynucleotidetriphosphate mixture in a procedure for directionally ligating a nucleic acid into a first adaptor sequence and a second adaptor sequence, wherein the adaptor sequences are duplex nucleotide sequences for cohesive ligation to an end of an exonuclease digested amplification product.

254. (previously presented) The kit of claim 253 further comprising:

(G) the first adaptor sequence, wherein the first adaptor sequence comprises a DYKDDDDK epitope tag; and

(H) the second adaptor sequence.

255. (previously presented) The kit of claim 254 wherein the modified deoxynucleotidetriphosphates consist of an alpha thiophosphorano dGTP and an alpha thiophosphorano dATP.

256. (previously presented) The kit of claim 255 wherein the first primer has a 5' terminus and the second primer has a 5' terminus.

257. (previously presented) The kit of claim 256 wherein the exonuclease is an exonuclease III.

258. (previously presented) The kit of claim 257 wherein at least one polymerase is a Taq polymerase or a recombinant Taq polymerase.

259. (previously presented) The kit of claim 258 wherein there are at least two polymerases.

REMARKS

Claims 186-211, 215-222, 229-259, and 228 remain pending. Claims 1-185, 212-214, and 223-227 have been cancelled. The Examiner has acknowledged that claims 229-259 are allowable. The Examiner has acknowledged that claims 186-211, 215-222, and 228 are objected to as being dependent on a base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

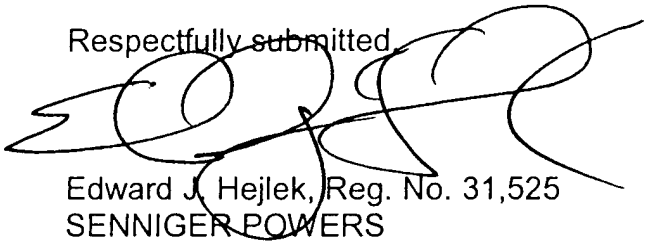
Claims 186, 206, and 215 have each been drafted in independent form to include all requirements of former base claim 159. Independent claim 229 and dependent claim 230 have been amended to place functional language at the end of the claim for enhanced readability, but the amendments do not change the scope of the claims. Independent claim 250 was amended to enhance readability but the scope of the claim remains unchanged.

CONCLUSION

Applicant appreciates the Office's thorough consideration of the subject application, as amended. In light of the foregoing, Applicants request an entry of the claim amendments and solicit allowance of the claims. The Office is invited to contact the undersigned attorney should any issue remain unsolved.

The Commissioner is hereby authorized to charge any underpayment and credit any overpayment of government fees to Deposit Account No. 19-1345.

Respectfully submitted,



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EXAMINER
HORLICK, KENNETH R

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/02/2005

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,292	11/15/2001	Brian Ward	SGM 6938.1	2146

TITLE OF INVENTION: RECOMBINANT DNA PROCESSES USING A DNTP MIXTURE CONTAINING MODIFIED NUCLEOTIDES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1400	$300	$1700	05/02/2005

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

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B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 12/04) Approved for use through 04/30/2007.

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000321 7590 02/02/2005 EJH / TBM / DJH

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EXAMINER	
HORLICK, KENNETH R	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/02/2005

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 159 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 159 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571) 272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

mmm

Notice of Allowability	Application No.	Applicant(s)	
	10/002,292	WARD ET AL.	
	Examiner	Art Unit	
	Kenneth R Horlick	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the response filed 01/20/05*.

2. ☒ The allowed claim(s) is/are *186-211, 215-222, and 228-259 (final claims 1-66)*.

3. ☒ The drawings filed on *11/15/01* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
   1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Kenneth R Horlick
Primary Examiner
Art Unit: 1637

1/31/05